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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,253	06/13/2001	Joseph Attila Rothnagel	13711	7342

7590 07/28/2004

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EXAMINER	
MCKELVEY, TERRY ALAN	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/880,253	ROTHNAGEL ET AL.	
	Examiner	Art Unit	
	Terry A. McKelvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,7,22-25,32-35,42-76,80-88 and 92-99* is/are pending in the application.

4a) Of the above claim(s) *2,22-25,33,34,44,52-74,76,80,88,92,93,97 and 99* is/are withdrawn from consideration

5)☒ Claim(s) *42,43 and 45-51* is/are allowed.

6)☒ Claim(s) *1,32,75,82-87,94 and 95* is/are rejected.

7)☒ Claim(s) *7, 35, 81, 96, 98* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All objections and rejections not repeated in the instant Action have been withdrawn due to applicant's response to the previous Action.

Election/Restrictions

Claims 2, 22-25, 33, 34, 44, 52-74, 76, 80, 88, 92, 93, 97, and 99 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/4/03 and 6/11/03.

This application contains claims 2, 22-25, 33, 34, 44, 52-74, 76, 80, 88, 92, 93, 97, and 99 drawn to an invention nonelected with traverse in the reply filed on 3/4/03 and 6/11/03. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 102

Claims 1, 32, 87, and 94-95 are rejected under 35 U.S.C. 102(b) as being anticipated by Reff (U.S. Patent No. 5,648,267). This rejection is maintained for reasons of record set forth in the paper mailed 12/4/03. Applicants' arguments filed 5/6/04 have been fully considered but they are not deemed to be persuasive.

Reff teaches to translationally impair the selectable marker of an expression vector, in order to improve the efficiency of protein expression (of the heterologous gene to be expressed by the vector in addition to the selectable marker) by significantly decreasing the number of viable colonies (column 3). This reference teaches creating a translationally impaired selectable marker gene by adding an ATG triplet upstream of the authentic ATG start site of the neo gene (claim 1; Figure 1). The intent of the added start codon is to, in effect, further impair translation of the selectable marker (column 12). This reference teaches that the cell line is preferably of mammalian origin (but does not exclude other eukaryotic cell lines), and specifically teaches human cell lines (column 15).

Response to Arguments

The applicant argues that Reff teaches impairment of the translation of a selectable marker gene requires a fully impaired Kozak sequence, but does not teach that the insertion of ATG codons in the 5' UTR of a gene alone, absent a fully impaired Kozak sequence, is sufficient to reduce translation of a downstream gene, and thus Reff does not teach or suggest the addition of an ATG codon as an independent means for downregulating translation, as claimed (unlike what the present application discloses).

In response to applicant's argument that the reference fails to show certain features of applicant's invention, it is noted that the feature upon which applicant relies (i.e., the addition of an ATG codon as an independent means for downregulating translation) is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claimed method is drawn to "... comprising introducing one or more ATG triplets ... upstream of ... authentic translation initiation site such that upon expression of said genetic sequence, there is a decrease in the level of expression." There is no claim limitation to the

addition of an ATG codon as an independent means for downregulating translation, especially as shown by the use of "comprising" in the claim and that the addition of ATP triplet(s) do not exclude addition of other nucleotides. There is no claim limitation concerning whether or not the Kozak sequence is impaired. The impaired Kozak sequence still constitutes an authentic translation site of an orf because impairment does not mean that the translation start site is not authentic or functional, otherwise the mechanism by which the impaired translation of the selectable marker is used, requiring plasmids which could overcome the impairment by over-production of the gene product, would not work. Reff et al literally meets all of the limitations of the claimed invention by teaching insertion of an ATG upstream of an authentic translation site of an orf which results in a decrease in the level of expression.

Claim Rejections - 35 USC § 103

Claims 1, 32, 75, 87, and 94-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reff (U.S. Patent No. 5,648,267) in view of Haselkorn et al (U.S. Patent No. 6,306,636 B1). This rejection is maintained for reasons of record set forth in the paper mailed 12/4/03. Applicants' arguments filed

5/6/04 have been fully considered but they are not deemed to be persuasive.

Reff teaches to translationally impair the selectable marker of an expression vector, in order to improve the efficiency of protein expression (of the heterologous gene to be expressed by the vector in addition to the selectable marker) by significantly decreasing the number of viable colonies (column 3). This reference teaches creating a translationally impaired selectable marker gene by adding an ATG triplet upstream of the authentic ATG start site of the neo gene (claim 1; Figure 1). The intent of the added start codon is to, in effect, further impair translation of the selectable marker (column 12). This reference teaches that the cell line is preferably of mammalian origin (but does not exclude other eukaryotic cell lines), and specifically teaches human cell lines (column 15).

Reff does not specifically teach translationally impairing a gene in plant cells.

Haselkorn et al teach that the upstream AUG codons (referring to the mRNA encoded by the gene, which is ATG in the gene itself) are believed to affect the efficiency of mRNA translation and as such may be important in the regulation of expression of some genes. They are also found in some plant mRNAs (column 37).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the translational impairing method taught by Reff by substituting the animal cells taught by Reff with plant cells because Haselkorn et al teaches that AUGs (corresponding to ATGs in the DNA) upstream of the start site affect translation, including in plants, and Reff teaches the general utility of translationally impairing selectable markers in order to increase expression of the other heterologous gene in the vector.

One would have been motivated to do so for the expected benefit of increasing the expression of heterologous genes in plant cells as taught by the combination of the cited references. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments

The applicant's arguments are directed to the alleged deficiencies of Reff, same as described above. These arguments are not persuasive for the same reason as addressed above. The applicant also argues that the Haselkorn et al reference does not cure the deficiencies of Reff. This argument is not

persuasive because Haselkorn et al was not relied upon to cure what the applicant alleges to be the deficiency of Reff. Haselkorn et al is merely relied upon to show that it would have been obvious to apply the teachings of Reff (which are directed to animal cells) to plant cells as taught by Haselkorn et al.

Claims 1, 32, 75, 82-87, and 94-95 rejected under 35 U.S.C. 103(a) as being unpatentable over Reff and Haselkorn et al as applied to claims 1, 32, 75, 87, and 94-95 above, and further in view of Engler et al (U.S. Patent No. 5,262,316) and Hansen et al (U.S. Patent No. 6,051,409).

Reff and Haselkorn et al are taught above and applied as before.

Reff and Haselkorn et al do not specifically teach the plant cell being from cotton or a cereal crop, or the target sequence whose expression is modulated confers resistance to a herbicide or pesticide.

Engler et al teaches transformation of plant cells and that exogenous genes to be introduced into plant cells include selectable plant marker genes to permit screening and selection of transformed cells and functional genes to be introduced and expressed in plants may be a structural gene which encodes a

polypeptide which imparts the desired phenotype, including herbicide resistance, pesticide resistance, etc (columns 5-6).

Hansen et al teach that plants can be transformed with any desired DNA fragment which the skilled artisan desires to have integrated into the cell genome such as one that expresses a protein of interest (column 12). The DNA fragment comprises appropriate regulatory sequences, including the leader sequence, which direct the expression of the gene in the DNA fragment (column 9). This reference teaches that the potential plant targets includes cotton and cereal plants (column 12).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method made obvious by the combined teachings of Reff and Haselhorn et al as taught above by using as the plant cells cereal crop or cotton cells as taught by Hansen et al or to use as the target sequence to be modulated a herbicide or pesticide resistance gene as taught by Engler et al because both Engler et al and Hansen et al teach that it is within the ordinary skill in the art to transform plant cells with an expressed gene encoding a desirable trait, Engler et al teach that the desirable trait can be herbicide or pesticide resistance gene, and Hansen et al teach that the plant cells can be cotton or a cereal crop.

One would have been motivated to do so for the expected benefit of making plant cells that more efficiently express a heterologous gene as taught by Reff, in plants as taught by the other cited references. One would have been specifically motivated to use the cells from specific crops because these are taught as target plants by Hansen et al, which are economically important. One would have been motivated to specifically reduce the resistance genes taught by Engler et al in order to reduce the expression of these genes to just the level needed for the desired resistance. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments

The applicant's arguments are directed to the alleged deficiencies of Reff and Haselkorn et al, same as described above. These arguments are not persuasive for the same reason as addressed above. The applicant also argues that the other secondary references do not cure the alleged deficiencies of Reff and Haselkorn et al. This argument is not persuasive because the secondary references were not relied upon to cure

what the applicant alleges to be the deficiencies of Reff and Haselkorn et al. The other secondary references are merely relied upon to show that it would have been obvious to apply the teachings of Reff and Haselkorn et al to the particular types of plant cells and target sequences as taught by the other secondary references.

Allowable Subject Matter

Claims 7, 35, 81, 96, and 98 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 703-872-9306. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

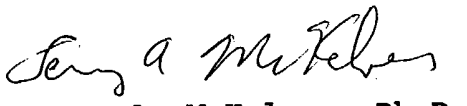
Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-

9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (571) 272-0775. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.



Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

July 24, 2004